REMARKS

In the Office Action, the Examiner rejected claims 1-20 under 35 U.S.C. § 112, second paragraph; rejected claims 1-20 under 35 U.S.C. § 112, first paragraph; rejected claims 1-20 under 35 U.S.C. § 102(b) as being anticipated by U.S. Patent No. 5,219,895 to Kelman et al.; rejected claims 1, 5-10, 11 and 15-20 under 35 U.S.C. § 102 as being anticipated by U.S. Patent Application Publication No. US2002/0022588 to Wilkie et al.; rejected claims 1-3 under 35 U.S.C. § 102 as being anticipated by U.S. Patent No. 6,197,934 to DeVore et al.; rejected claims 1-20 under 35 U.S.C. § 103(a) as being unpatentable over Kelman et al., DeVore et al., and U.S. Patent No. 6,495,127 Wallace et al.; rejected claims 1-20 under 35 U.S.C. § 103(a) as being unpatentable over Wilkie et al. in view of Kelman et al. and DeVore et al.; rejected claims 1-20 under 35 U.S.C. § 103(a) as being unpatentable over DeVore et al. in view of Wilkie et al., Wallace et al., Kelman et al. and U.S. Patent No. 6,161,544 to Devore et al. ("Devore '544"); and rejected claims 1-20 under the judicially created doctrine of obviousness-type double patenting.

Applicants have amended claims 2, 4, 5, 7, 10, 12, 14, 17, and 20; cancelled claims 1, 6, 8, 11, 16 and 18; and added new claims 21-26. Claims 2-5, 7, 9, 10, 12-15, 17, and 19-26 are pending in the present application.

At the outset, Applicants draw the Examiner's attention to new claims 21-26, which have been added in this Amendment. New independent claim 21 recites a method of making a tissue adhesive

comprising the steps of adding a first collagen portion to a second collagen portion to obtain a mixture including the first and second collagen portions. Claim 21 further recites a step of heating the mixture to thereby obtain a desired collagen concentration. The desired collagen concentration is at least 300 mg/ml but not more than 800 mg/ml. Exemplary support for new claim 21 may be found in the specification at page 10, line 18 - line 11, line 1, which describes successively adding lyophilized or dried collagen (any one of such added collagen portions corresponding, for example, to the claimed "first collagen portion") to a collagen mixture of approximately 50 mg/ml which has been heated to cause gelatinazation (corresponding, for example, to the claimed "second collagen portion"). The cited portion of the specification further discloses exposing a solution including the lyophilized or dried collagen and the gelatinized collagen to "microwave energy" (corresponding to the claimed step of "heating said mixture"). According to the specification at page 10, lines 15-16 (see also page 3, line 7), the disclosed technique can achieve compositions having a total collagen concentration of 30-80% (corresponding to the claimed limitation of obtaining a desired collagen concentration associated with the mixture that is "at least 300 mg/m but not more than 800 mg/ml"). Both derivatized and non-derivatized collagen may be used in connection with the present invention (see page 10, lines 2-4).

New independent claim 23 recites steps of adding additional collagen to a mixture including collagen, and heating the mixture including the additional collagen. The cited portion of the

specification describing addition of lyophilized or dried collagen to a gelatinized collagen provides exemplary support for these limitations. New claim 23 also requires repeating the adding and heating steps to obtain a desired collagen concentration that is at least equal to 300 mg/ml but not more than 800 mg/ml. Exemplary support for the repeating steps may be found in the specification at page 10, line 23 - page 11, line 1, which states that "[t]his sequence [of adding collagen and heating] continued until the desired collagen concentration was attained." New claims 22 and 24 depend from claims 21 and 23, respectively, and further recite derivatization of the supplied first collagen (new claim 22) and the additional collagen (new claim 24) with a function group selected from COO^- and SH^-. Applicants respectfully point out that the Examiner acknowledges that derivatization with COO^- and SH^- groups are described in the specification (see Office Action at page 6), and thus new claims 22 and 24 are believed to be supported by the disclosure in light of the Examiner's comments.

New claims 25 and 26, which depend from claims 21 and 23, respectively, recite solidifying the mixture and sectioning the solidified mixture into strips. Support for new claims 25 and 25, may be found in the specification, for example, at page 11, lines 4-5, which describes "solidified gelatinized collagen films [that] were sectioned into strips … ."

Accordingly, Applicants respectfully submit that new claims 21-26 are adequately supported by Applicants' disclosure.

Applicants respectfully traverse the Examiner's rejections of

claims 1-20 under 35 U.S.C. § 112, second paragraph. Applicants have amended claim 5 to clarify its dependency from claim 4. Although Applicants respectfully disagree with the positions taken by the Examiner in the Office Action with respect to the § 112, second paragraph rejection, Applicants have cancelled claims 1, 6, 11 and 16, upon which the Examiner's rejection was premised, and therefore submit that the rejection is moot. Applicants respectfully request the Examiner to reconsider and withdraw the rejection under 35 U.S.C. § 112, second paragraph.

Applicants respectfully traverse the Examiner's rejection of claims 1-20 under 35 U.S.C. § 112, first paragraph, and submit that the Examiner's rejection is moot with respect to cancelled claims 1, 6, 8, 11, 16 and 18. Moreover, although Applicants respectfully disagree with the arguments set forth the Examiner in formulating the rejection under § 112, first paragraph, Applicants appreciate the Examiner's comments, and have drafted selected new claims in light of the Examiner's proposals.

As discussed above, each of new claims 21-26 is adequately supported by Applicants' disclosure, including new independent claims 21 and 23. Further, consistent with the Examiner's proposal at page 5 of the Office Action, claims 21 and 23 are directed toward a tissue adhesive. In addition, new claims 21 and 23 require a mixture having a collagen concentration of at least 300 mg/ml but not more than 800 mg/ml, a feature that the Examiner concedes is adequately described in the specification (see pages 7 and 8 of the Office Action).

In addition, as noted above, in light of the Examiner's

acknowledgement of support in the specification for collagen derivatized with COO^- and SH^- functional groups, Applicants submit that new claims 22 and 24, which recite the step of derivatizing a first collagen portion (claim 22) and an additional collagen portion (claim 24) with a functional group selected from COO^- and SH^-, are supported by the Applicants' disclosure. Moreover, Applicants have amended claims 7 and 17 to recite the suggested pH range set forth by the Examiner at page 9 of the Office Action. Claims 8 and 18, which previously recited this range, have been cancelled in order to maintain proper antecedent basis.

Accordingly, Applicants respectfully submit that pending claims 2-5, 7, 9, 10, 12-15, 17, and 19-26 meet the requirements of 35 U.S.C. § 112, first paragraph.

Applicants respectfully traverse the Examiner's rejection of claims 1-20 under 35 U.S.C. § 102(b) as being anticipated by Kelman et al.; rejection of claims 1, 5-10, 11 and 15-20 under 35 U.S.C. § 102 as being anticipated by Wilkie et al.; rejection of claims 1-3 under 35 U.S.C. § 102 as being anticipated by DeVore et al.; rejection of claims 1-20 under 35 U.S.C. § 103(a) as being unpatentable over Kelman et al., DeVore et al., and Wallace et al.; rejection of claims 1-20 under 35 U.S.C. § 103(a) as being unpatentable over Wilkie et al. in view of Kelman et al. and DeVore et al.; rejection of claims 1-20 under 35 U.S.C. § 103(a) as being unpatentable over DeVore et al. in view of Wilkie et al., Wallace et al., Kelman et al. and Devore et al. ("Devore '544"); and the rejection of claims 1-20 under the judicially created doctrine of obviousness-type double patenting. Applicants

respectfully submit that the Examiner's rejections are moot in light of the cancellation of independent claims 1 and 11, as well as dependent claims 6, 8, 16 and 18. Moreover, to the extent the Examiner's rejections are pertinent to new independent claim 21, Applicants respectfully submit that none of the applied references teaches or suggests each and every step recited in the claim. In particular, the applied prior art at least fails to teach the claimed method including the steps of adding a first collagen portion to a second collagen portion to obtain a mixture including the first and second collagen portions, and heating the mixture to thereby obtain a desired collagen concentration that is at least equal to 300 mg/ml but not more than 800 mg/ml.

Specifically, although Kelman et al. is directed toward collagen-based adhesives, the reference is silent as to adding a first collagen portion to a second collagen portion, as required by claim 21. Moreover, Kelman et al. teaches, for example, "[a]n effective amount of sulfonating agent is broadly from about 0.5 to 20% wt total collagen ..." (col. 4, lines 63-65). Applicants respectfully submit, however, that such teachings fall short of disclosing or rendering obvious Applicants claimed heating step to thereby obtain a desired concentration of collagen that is at least equal to 300 mg/ml but not more than 800 mg/ml.

With respect to Wilkie et al., the Examiner contends that Example 5 at page 18 and the last sentence at page 6 of the reference discloses "derivatizing collagen (700 mg; 20-45%) ... wherein the resulting solution may be titrated ... and may also be heated." (see Office Action at page 11). New claim 21 requires

adding a first collagen portion to a second collagen portion to obtain a mixture. Wilkie et al. in Example 5 discloses adding 7 grams of derivatized collagen to a solution containing perfluorooctanoic acid, phosphate buffer and NaOH. Wilkie et al. does not disclose adding the derivatized collagen to another portion of collagen, as required by new claim 21.

Moreover, while Wilkie et al. discloses "20-45% derivatized collagen", Applicants submit that the described percentage defines an amount of derivatization of the collagen, but not a concentration of collagen itself, in units of mg/ml. Applicants further note that in Example 5, 7 grams of derivatized collagen are added to the buffered solution described above on a "100 g scale" (see paragraph 0289) to obtain "a sealant composition based on 7% collagen". Accordingly, Example 5 only teaches adding 7 grams of derivatized collagen to a non-collagen solution to obtain a total of 100 grams of material having an overall concentration of 7%. In contrast, new claim 21 requires adding a first collagen portion of collagen to a second collagen portion, heating a mixture including the first and second portions of collagen to obtain a desired collagen concentration associated with the mixture which is at least equal to 300 mg/ml but not more than 800 mg/ml. Wilkie et al. fails to disclose these steps.

Further, although Wilkie et al., at page 6, discloses heating albumin to increase the viscosity thereof, Applicants submit that the reference fails to suggest heating the composition described in Example 5. Even if Wilkie et al. suggests heating the Example 5 composition, however, the reference nevertheless is silent as to

the resulting collagen concentration that is at least equal to 300 mg/ml but not more than 800 mg/ml, as recited in new claim 21.

In formulating the Section 102 rejection based on DeVore et al. (U.S. Patent No. 6,197,934), the Examiner asserts that "Devore et al. teach heating [and additional heating] a derivatized [COO-] collagen (column 1, lines 44-47), to a pH of 7.4 (column 4, line 31) and the use of NaOH as a pH altering material (column 4, line 22). Applicants note, however, that the cited portion of DeVore et al. at column 1 only states a single derivatized collagen heating step, not additional heating, as alleged by the Examiner. In any event, DeVore et al. discloses adding "a therapeutic compound" such as mitomycin, an anti-metabolic antibiotic, to the heated derivatized collagen (col. 1, lines 41-47, and 63-65). There is no teaching in DeVore et al. of the step of adding a first collagen portion to a second collagen portion, as recited in new claim 21. In addition, DeVore et al. apparently discloses dissolved collagen in a solution having a "concentration of 10 mg/ml" (see col. 4, lines 29-33), well below the claimed concentration of at least 300 mg/ml but not more than 800 mg/ml, as recited in new claim 21.

The Examiner also contends portions of Devore et al. ('544) teach use of 4-mercapto-1,8-naphthalic anhydride (the "Anhydride"), and that claims 4 and 14, which recites reaction with the Anhydride are thus obvious. The Examiner further relies on teachings in Wallace et al. of microfibrillar and fibrillar collagen in arguing that claims 10 and 20 are obvious as well. Applicants respectfully submit, however, that even if the cited

portions of Devore et al. and Wallace et al. were combinable with any of the other references relied upon by the Examiner in the above-noted rejections, the resulting combination of references would still fail to teach the method recited in new claim 21. Namely, none of the cited references teaches a method of adding a first collagen portion to a second collagen portion to obtain a mixture, and heating the mixture to obtain an associated desired collagen concentration, which is at least equal to 300 mg/ml, but not more than 800 mg/ml.

With respect to the Examiner's double patenting rejection, the Examiner asserts that claims 4, 17 and 24 of Kelman et al. in combination with "DeVore et al." (Applicants are unclear which of the two cited DeVore references the Examiner relies upon in the double patenting rejection) and Wallace et al. render claims 1-20 unpatentable. Claims 4, 17 and 24 are directed toward a collagen composition wherein Type 1 collagen is derived from human tissue or animal tissue (claim 4, which depends from claim 1); a method of making a collagen composition including steps of, in part, preparing partially fibrillar collagen and reacting the partially fibrillar collagen with at least one of an acylating agent and sulfonating agent at a pH ranging from 7.5 to 10.0 and a temperature ranging from 4°C to 37° C (claim 17); and the method, in part, wherein the acylating agent is glutaric anhydride (claim 24, which depends from claim 23, which in turn depends from claim 17). None of these claims recites the claimed method of new claim 21 including adding first and second collagen potions to obtain a mixture, and heating the mixture to obtain the desired solder

concentration. Since, as noted above, both Devore references and Wallace et al. also fail to teach or suggest the method recited in new claim 21, Applicants submit that the claim is patentable over claims 4, 17 and 24 taken in combination either Devore reference and Wallace et al.

New claim 23 is similar to new claim 21, in that it recites steps of adding additional collagen to a mixture including collagen, and heating the mixture including the additional collagen. New claim 23 further requires, however, repeating the adding and heating steps to obtain a desired collagen concentration that is at least equal to 300 mg/ml but not more than 800 mg/ml. This claimed range of desired collagen concentrations is also recited in new claim 21. Accordingly, new claim 23 is distinguishable over the applied references at least for reasons discussed above in regard to new claim 21.

In light of the above-described deficiencies of the applied references, Applicants submit that new claims 21 and 23 are allowable over Kelman et al. including claims 4, 17 and 24 of Kelman, Wilkie et al., DeVore et al., Wallace et al., Devore '544. In addition, claims 2-5, 7, 9, 10, 22 and 25 are allowable at least due to their dependence from claim 21; and claims 12-15, 17, 19, 20, 24 and 26 are allowable at least due to their dependence from claim 23.

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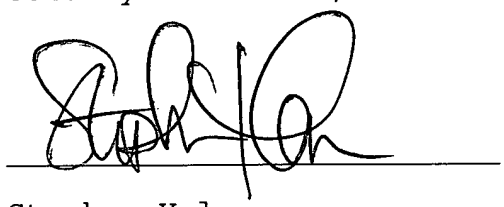
Respectfully submitted,

By: 

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